25. (Twice Amended) The formulation of claim 2, wherein component a) is selected from cyclosporins cyclosporin A, cyclosporin D and cyclosporin G, wherein the ratio of components a: c is 1.001: 1 to 1.5 : 1.

27. (Twice Amended) The formulation of claim 2, further comprising a taxane.

29. (Twice Amended) The formulation of claim 27, wherein the taxane is docetaxel or paclitaxel.

31. (Twice amended) A dosage form containing a formulation according to claim 2.

Proposed new claims 33 and 34 do not add new matter. Support for proposed new claims may be found in the specification at, for example, at page 7, lines 26-29, and at page 7 lines 30-31. Support for amended claims 25 and 27 may be found at page 7, lines 16-17. Support for amendments of claims 29 and 31 is found for example at page 8, lines 23 and 24.

A marked-up version of the amended claims pursuant to 37 C.F.R. § 1.121(c)(1)(ii) is attached separately as Exhibit A.

REMARKS

Applicants respectfully request reconsideration of the rejections set forth in the Action mailed on April 19, 2002. Claims 2, 25, 27, 29, and 31 have been rejected. Claims 1, 3-24, 26, 28, 30, and 32 have been withdrawn from consideration. Claims 33 and 34 have been added herein.

Applicants note, with appreciation, that the rejection under 35 U.S.C. § 112, first paragraph as applied to claims 2, 25, 27, and 29 has been withdrawn.

This amendment is to expedite prosecution and should not be construed as acquiescence in any ground of rejection. Applicants reserve the right to prosecute the originally filed claims in the future. A clean version of the amended claims with instructions for entry pursuant to 37 C.F.R. § 1.121(c)(1)(i) is included above. The comments in the Action are now addressed in turn.

Claim Rejections under 35 U.S.C. § 112, first paragraph

Claim 31 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such as way as to enable one skilled in the art to make and/or use the invention. The Examiner has expressed specific concerns regarding the term "pharmaceutical". The Examiner has provided several suggestions as to alternative claim language which have been adopted in newly introduced claims.

Although Applicants maintain that the claim is enabled, and thus traverse this rejection, to expedite prosecution of this particular application in its present form and to further the business interests of Applicant, the claim has been amended herein in accordance with the Examiner's suggestion. Applicants respectfully request withdrawal of the rejections presently on the record under 35 U.S.C. § 112, first paragraph and reconsideration of claim 31 in its amended form.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claim 31 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and claim the invention. The Examiner has also set forth specific rejections to the form of claims 25, 27, and 29. The claims have been amended herein to address the Examiner's concerns. Applicants respectfully request withdrawal of the rejections presently on the record under 35 U.S.C. § 112, second paragraph and reconsideration of the claims in their amended form.

Claim Rejections under 35 U.S.C. § 103(b)

The claims have been rejected under 35 U.S.C. § 103(b) as being unpatentable over PCT WO 98/10747 ("Stuchlik"). The rejection is respectfully traversed as applied to the claims as amended herein.

The presently claimed invention is drawn to a formulation of one or more cyclosporins admixed with (1) various polyglycerol esters of fatty acids and (2) one or more triglyceride macrogol glycerol esters, partial glycerides of fatty acids and macrogol esters of fatty acids. Upon dilution with water, the viscosity of the formation increases by at least 5 times in comparison with the undiluted composition. In addition, the formulation forms a

dispersion of polymorphous gel particles having a dimension of 0.2 to 500 μm. Surprisingly it has been found that these gel particles have a non-spherical character. See, Figures. It is thought that this non-spherical character contributes, at least in part, to the resulting high bioavailability of the cyclosporins in the formulation. See, e.g., Specification at page 6.

Stuchlik is cited as teaching compositions comprising cyclosporin and polyglycerol esters. The Examiner conceded that Stuchlik does not disclose the specific ratios of components. Moreover, Stuchlik does not teach or suggest any methods for preparing nonspherical particles, as claimed herein. Stuchlik does not teach or suggest that such nonspherical particles would be desirable. Indeed, Stuchlik teaches that methods for preparation of "homogeneously dispersed substance". See, e.g., Stuchlik at page 6 and 7.

Applicants assert that by suggesting that the cited art may be used to produce the presently claimed invention, the Examiner presents, in essence, an "obvious to experiment" or "obvious to try" standard for obviousness. The "obvious to try" standard has been thoroughly discredited by the courts. Indeed, an obviousness rejection is inappropriate, where the prior art gives no indication of which parameters are critical or no direction as to which of many choices is likely to be successful. *In re O'Farrell*, 7 USPQ2d 1673, 1681 Fed. Cir. 1988. "Both the suggestion and the expectation of success must be founded in the prior art, and not in applicant's disclosure." *In re Dow Chemical*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). There is simply no suggestion in the cited reference regarding the advantages in formulations comprising non-spherical particles or methods for their preparation. Thus, there is nothing in the cited prior art that would provide one of ordinary skill in the art with the knowledge necessary to develop the claimed inventions.

For these reasons, withdrawal of the rejections is respectfully requested.

Conclusion

On the basis of the above remarks, this application is believed to be in condition for allowance. Accordingly, reconsideration of this application and its allowance are requested.

A request for a Three (3) Month Extension of Time, up to and including October 21, 2002 is included herewith. Pursuant 37 C.F.R. § 1.136(a)(3), the Examiner is authorized to charge any fee under 37 C.F.R. § 1.17 applicable in the instant, as well as in future

communications, to Deposit Account No. 50-0943. Such an authorization should be treated as a constructive petition for extension of time in the concurrent as well as future replies.

The Examiner is encouraged to call the undersigned to facilitate prosecution.

Respectfully submitted,
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

(Case No. GAL060175-US)

In re Application of:	Andrysek *et al.*	) Examiner: Lukton, David
Serial No.:	09/642,242	) Art Unit: 1653
Filed:	August 17, 2000	)
For:	PHARMACEUTICAL COMPOSITIONS FOR ORAL AND TOPICAL ADMINISTRATION	)

EXHIBIT A

Marked-Up Version of Amendments

2. (Three Times Amended) A formulation for oral or topical administration including

a) one or more cyclosporins;

b) 5 to 50% of one or more compounds selected from polyglycerol esters of fatty acids of formula (1)

$$CH_2OR\text{-}CHOR\text{-}CH_2O\text{-}(CH_2CHOR\text{-}CH_2O\text{-})_nCH_2\text{-}CHOR\text{-}CH_2OR \quad (1)$$

wherein n is an integer from 4 to 13 and R is H or CO_2R' wherein R' is $C_{8\text{-}22}$ saturated, unsaturated or hydroxylated alkyl and wherein at least one group R is not hydrogen;

c) 5 to 50% of one or more compounds selected from polyglycerol esters of fatty acids and/or unsaturated fatty acids of formula (2)

$$CH_2OR\text{-}CHOR\text{-}CH_2O\text{-}(CH_2CHOR\text{-}CH_2O)_nCH_2\text{-}CHOR\text{-}CH_2OR \quad (2)$$

wherein n is an integer from 0 –10 and R = H or CO_2R'' wherein R" is $C_{8\text{-}22}$ saturated, unsaturated or hydroxylated alkyl, and wherein at least one group R is not hydrogen;

d) 5 to 50% of one or more compounds selected from the group consisting of triglyceride macrogol glycerol esters, partial glycerides of fatty acids and mac[g]rogol esters of fatty acids in which the average quantity of reacted ethylene oxide in the synthesis of these

substances ranges between 50 to 150 mols and concurrently the ratio between components b) and d) is from 0.1:1 to 10:1;

wherein the above percentages are selected to total 100%;

[and] wherein upon dilution with water 1:1 by volume the viscosity of the formulation increases by at least 5 times in comparison to the undiluted composition; and

wherein upon dilution with water the formulation forms a dispersion of non-spherical polymorphous gel particles having a dimension of 0.2 to 500 µm.

25. (Twice Amended) [A] The formulation [as claimed in] of claim 2, wherein component a) is selected from cyclosporins cyclosporin A, cyclosporin D [or] and cyclosporin G, wherein the ratio of components a: c [+ e] is 1.001: 1 to 1.5 : 1.

27. (Twice Amended) [A] The formulation [as claimed in] of claim 2, [wherein component a) is selected from taxanes docataxel or paclitaxel, wherein the ratio of components a :c + e is 0.001:1 to 1.5:1] further comprising a taxane.

29. (Twice Amended) [A] The formulation [as claimed in] of claim 27, wherein [component a) includes at least one compound selected from the group comprising cyclosporins and further at least one compound selected from the group comprising taxanes] the taxane is docetaxel or paclitaxel.

31. (Twice amended) A [pharmaceutical] dosage form [comprising a gelatin capsule] containing a formulation [as claimed in] according to claim 2.